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Cohort-specific trends in stroke mortality in seven European countries were related to infant mortality rates

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Abstract

Objectives: To assess, in a population-based study, whether secular trends in cardiovascular disease mortality in seven European countries were correlated with past trends in infant mortality rate (IMR) in these countries.

Study Design and Setting: Data on ischemic heart disease (IHD) and stroke mortality in 1950–1999 in the Netherlands, England & Wales, France, and four Nordic countries were analyzed. We used Poisson regression to describe trends in mortality according to birth cohort, for the cohorts born between 1860 and 1939. Pearson correlation coefficients were calculated to determine associations between IMR and IHD, or stroke mortality.

Results: IHD mortality increased for successive cohorts up to 1900, and then started to decline. Stroke mortality levels were virtually stable among birth cohorts up to 1880, but declined rapidly among later cohorts. A strong positive association was found between cohort-specific IMR levels and stroke mortality rates. There were no strong cohort-wise associations between IMR and IHD mortality.

Conclusion: These results support other studies in suggesting that living conditions in early childhood may influence population levels of stroke mortality. Future studies should determine the contribution of specific early life factors to the mortality decline in IHD and especially stroke.

Keywords: Europe; Mortality trends; Ischemic heart disease; Stroke; Cohort analysis; Infant mortality rate

1. Introduction

Although several studies have shown that the risk of ischemic heart disease (IHD) is associated with adverse living conditions in early life [1–5], this finding has not always been able to be consistently replicated [6,7]. For stroke, some studies have observed a relation with living conditions in early life [4,8], whereas others have not [2,5]. The ''fetal origin'' hypothesis [9,10] states that the risk of stroke is increased by maternal influences associated with poverty [9], a hypothesis, however, that is contested by others [11,12]. Similarly, population-based studies have suggested that early life factors may be important determinants of the trends and geographical differences in mortality from cardiovascular disease in adults [7,13–17]. For example, studies have shown a strong geographical correlation between mortality from various causes of death in adulthood and infant mortality around the time of birth, where infant mortality rate (IMR) was taken to reflect living conditions in early life [7,13–17]. One study observed that geographical differences in mortality from stroke in the late 20th century were correlated more strongly with infant mortality rates in the early 20th century than with current socioeconomic conditions [13].

Previous studies have reported declining trends of IHD for developed countries over recent decades [18–24], while the decline in stroke mortality rates between 1970 and 1990 slowed to a stop for both sexes and all ages [25]. Some studies assessed the effect of living conditions in early life on time trends (instead of geographical differences) in adult mortality [26,27]. These studies focused on the question of whether time trends in adult mortality reflect cohort effects or period effects. A period effect is evident when a similar (approximately parallel) shift in rates is seen in each age group during a particular calendar period, while a cohort effect is manifested by age-specific rates that rise and fall in parallel when plotted against year of birth (cohort) [26]. Cohort effects would be suggestive of effects located

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in early life, but clear evidence for such effects was lacking in most studies [27].

In this paper, we present results of a population-based time-series study that aimed to describe trends in mortality between subsequent cohorts in relation to living conditions in early life of these cohorts. We assessed cohort-wise trends of IHD and stroke mortality of populations in seven European countries, and determined whether these trends were correlated with developments in IMR at the time of birth of the subsequent cohorts. We addressed three research questions: (1) What are the trends in age- and sex-specific mortality from IHD and stroke in seven European countries between 1950 and 1999? (2) What are the trends according to birth cohort? (3) Do these cohort-wise trends coincide with trends in infant mortality rates in subsequent cohorts from 1860 to 1939?

2. Methods

We obtained data on IHD, stroke mortality, and population at risk, by year of death (1950–1999), sex, and 5-year age group for seven low-mortality European countries, i.e., Denmark, England & Wales, Finland, France, the Netherlands, Norway, and Sweden. For Denmark, Finland, and Norway data were available only from 1951, and for Sweden, from 1952. For France, data were only available until the year 1997 and for Denmark, until 1998. The data were obtained from national statistical offices and related institutes. See Janssen et al., 2004 [28] for more information.

In reconstructing mortality trends from IHD and stroke over the period from 1950 to 1999, we first ran up against the fact that the International Classification of Diseases (ICD-6 to ICD-10) had been revised five times during this same period. To reconcile these differences, we constructed a general concordance table, in which the different codes for stroke and for IHD in the successive ICD revisions were linked [28]. For IHD, we selected the ICD codes 420 and 422.1 for ICD-6 and ICD-7, 410–414 for ICD-8 and ICD-9, and I20–I25 for ICD-10. For cerebrovascular diseases we selected ICD codes 330–334 for ICD-6 and ICD-7, 430–434 and 436–438 for ICD-8 and ICD-9, and I60–I69 for ICD-10 [28,29]. For IHD, the numbers of deaths for code 422.1 under ICD-6 and ICD-7 were not available for Finland until 1963, and Sweden until 1961. We estimated these on the basis of the ratio of the number of deaths from IHD with and without 422.1, calculated for the first year in which 422.1 was coded.

Remaining mortality discontinuities—caused by the use of three-digit instead of four-digit codes and by incidental changes in coding rules—were identified and adjusted for in our analysis (see Janssen and Kunst (2004) for more information) [29]. We adjusted the person-years for the incidental changes in coding rules for stroke in 1956–58 for Finland, and for the generally applied coding changes in England and Wales between 1984 and 1992 [29]. We made adjustments for the mortality discontinuity in IHD due to the ICD revision from ICD-8 to ICD-9 in The Netherlands, and for the incidental changes in coding rules from 1970 onwards for Sweden [29].

Data on infant mortality rates (IMR), defined as the number of deaths during the first year of life per 1000 live-born babies, for the period 1860–1969 were obtained from Mitchell for most countries [30], and from Turpeinen for Finland [31].

To describe trends in mortality between 1950 and 1999, age-adjusted mortality rates by 10-year intervals were calculated using direct standardization, taking the age-specific person-years of each country in the 1950s as standard. For describing trends over time, we looked at two periods: from the 1950s to the 1970s (measured by age-adjusted mortality rate of 1970s divided by the age-adjusted mortality rate of 1950s) and from the 1970s to the 1990s (measured in similar ways).

To describe mortality differences between birth cohorts 1860 and 1939, we analyzed the mortality data by means of a log-linear regression analysis (Poisson regression). The dependent variable was the number of deaths, with the person-years at risk as offset variable. We included age and cohort (1-year intervals in Table 1 and 5-year intervals in Tables 2–4) as independent variables. Table 3 illustrates the mortality rates in each 5-year birth cohort relative to the mortality rates in cohort 1900–1904, thus enabling comparisons of the mortality rates between different cohorts to be made. These relative cohort mortality measures were derived from the parameter estimates of the cohort variable in the regression analysis.

Only age was controlled for in these cohort analyses. In subsequent analyses, however, we also controlled for "drift," the common linear trend, and nonlinear period effects [32,33] and found basically the same patterns of cohort differences in mortality as those shown below.

Pearson correlation coefficients were calculated in order to quantify associations between cohort-specific mortality levels and the level of IMR of each birth cohort. These correlations were estimated by comparing cohorts within countries. In addition, a pooled analysis was made combining all birth cohorts for all countries together. We restricted all analyses to cohorts born between 1860 and 1939, thus excluding birth cohorts with too few deaths during the observation period. Additional analyses, with further restriction to birth cohorts born between 1875 and 1924, showed similar results to those reported below.

We used SPSS for Windows (version 10.1), Excel for Windows (2000), and SAS version 8.0.

3. Results

Table 1 shows changes in mortality according to period of death, comparing the 1950s to the 1970s and the 1970s to the 1990s. IHD mortality generally increased between the 1950s and 1970s in all countries for both men and women, except for women in France and Finland below

Table 1
Trends in mortality from IHD and stroke in seven European countries between the 1950s and the 1990s, by age and sex

		Rate ratio comparing second to first period[a]							
		IHD				Stroke			
		Male		Female		Male		Female	
Country	Age group	1970s to 1950s	1990s to 1970s	1970s to 1950s	1990s to 1970s	1970s to 1950s	1990s to 1970s	1970s to 1950s	1990s to 1970s
Denmark	<45	1.8	0.5	2.1	0.4	1.1	0.9	1.2	0.9
	45–64	1.6	0.5	1.3	0.6	0.7	0.8	0.5	0.8
	65–79	1.6	0.6	1.1	0.6	0.6	0.7	0.4	0.7
	80+	1.7	0.7	1.4	0.6	0.6	0.8	0.6	0.8
England & Wales	<45	1.7	0.4	1.2	0.5	0.9	0.6	1.0	0.6
	45–64	1.5	0.5	1.1	0.7	0.7	0.5	0.7	0.4
	65–79	1.2	0.7	1.0	0.8	0.8	0.5	0.8	0.5
	80+	1.1	0.8	1.0	0.8	0.9	0.6	1.1	0.6
Finland	<45	1.2	0.3	0.8	0.4	1.1	0.4	0.9	0.4
	45–64	1.6	0.4	1.2	0.4	0.8	0.5	0.6	0.4
	65–79	1.5	0.7	1.4	0.7	0.8	0.6	0.6	0.5
	80+	1.5	1.0	1.3	1.0	0.8	0.6	0.8	0.6
France	<45	1.8	0.8	0.7	0.8	0.7	0.6	0.6	0.6
	45–64	1.4	0.6	1.0	0.5	0.6	0.4	0.4	0.4
	65–79	1.6	0.7	1.5	0.6	0.7	0.4	0.6	0.3
	80+	2.2	1.0	2.4	1.0	1.0	0.5	1.0	0.5
Netherlands	<45	2.4	0.5	1.4	0.7	1.3	0.6	1.6	0.7
	45–64	2.0	0.5	1.1	0.7	0.9	0.6	0.7	0.5
	65–79	1.6	0.6	1.1	0.6	0.8	0.6	0.7	0.5
	80+	1.4	0.8	1.2	0.7	0.8	0.7	0.8	0.7
Norway	<45	2.0	0.5	1.2	0.7	1.2	0.5	1.3	0.5
	45–64	1.8	0.5	1.2	0.7	0.8	0.6	0.6	0.5
	65–79	1.8	0.7	1.3	0.6	0.9	0.6	0.8	0.5
	80+	1.8	0.8	1.5	0.7	1.0	0.7	1.0	0.6
Sweden	<45	1.7	0.6	1.4	0.8	0.9	0.5	0.9	0.4
	45–64	1.5	0.5	1.1	0.6	0.7	0.6	0.4	0.5
	65–79	1.6	0.6	1.1	0.5	0.6	0.7	0.5	0.6
	80+	1.5	0.6	1.2	0.5	0.7	0.8	0.7	0.8

Abbreviation: IHD, ischemic heart disease.
[a] Calculated as standardized death rate of the second period divided by standardized death rate of the first period.

45 years. These increases were generally followed by a decline in IHD mortality in all countries between the 1970s and 1990s. The latter decreases were larger among younger people. Mortality from stroke declined from the 1950s to the 1990s in all age groups in most countries, often with larger declines in more recent decades.

Table 2 shows trends in mortality by year of birth from 1860 to 1939, subdivided into four segments, with each segment covering 20 years (1860–1879, 1880–1899, 1900–1919, and 1920–1939). Mortality from IHD generally increased with increasing year of birth between 1860 and 1899, at which point it started to decline. The reversal from increasing to decreasing IHD levels was more marked in France, Finland, and Norway than in other countries. In many countries, the decline started earlier among women than among men. Stroke showed a more consistent pattern of decreasing mortality in most populations, after initial increases in many countries for the birth cohorts 1860–1879. The rate of the decline in stroke mortality greatly differed according to birth period, country, and sex, with mostly higher declines for the youngest birth cohorts.

Figure 1 shows the trends by 5-year birth cohort in IHD, stroke, and infant mortality. IHD mortality increased between successive cohorts up to those born in about 1900, and then started to decline. Increased stroke mortality levels were relatively stable in birth cohorts up to 1880, but declined rapidly in subsequent cohorts. IMR showed a general tendency to decline, especially after 1900, a tendency that started much later in some countries (e.g., Denmark and England & Wales) than in others (e.g., The Netherlands). The irregularities in the decline in IMR do not clearly correspond to similar irregularities in the decline in stroke.

Table 3 shows the correlation coefficients comparing the cohort-specific levels of IMR with mortality trends from stroke or IHD at adult age for the subsequent cohorts. A variable and sometimes inverse relationship between IHD

Table 2
Trends in mortality from IHD and stroke over subsequent 20-year birth cohorts from 1860 to 1939 in seven European countries, by sex

		Annual change in mortality (%)			
		IHD		Stroke	
Country	Birth cohorts	Male	Female	Male	Female
Denmark	1860–1879	+3.76[a]	+4.30[a]	−0.79[a]	+0.13[a]
	1880–1899	−0.14[a]	−0.22[a]	−3.02[a]	−4.21[a]
	1900–1919	−0.35[a]	−1.22[a]	−1.14[a]	−1.72[a]
	1920–1939	−2.90[a]	−1.48[a]	−0.43[a]	−0.91[a]
England & Wales	1860–1879	−0.38[a]	−0.12[a]	+1.12[a]	+1.59[a]
	1880–1899	+0.10[a]	−0.96[a]	−3.06[a]	−3.27[a]
	1900–1919	−0.05[a]	−0.43[a]	−2.02[a]	−2.18[a]
	1920–1939	−2.96[a]	−2.19[a]	−3.00[a]	−3.58[a]
Finland	1860–1879	+2.41[a]	+2.38[a]	+1.78[a]	+2.10[a]
	1880–1899	+1.22[a]	+0.40[a]	−3.47[a]	−4.64[a]
	1900–1919	+0.05	−1.05[a]	−1.65[a]	−2.61[a]
	1920–1939	−4.69[a]	−4.80[a]	−2.63[a]	−4.11[a]
France	1860–1879	+5.90[a]	+7.57[a]	+2.48[a]	+3.19[a]
	1880–1899	+1.80[a]	+1.13[a]	−3.82[a]	−4.03[a]
	1900–1919	−0.49[a]	−2.23[a]	−2.91[a]	−4.01[a]
	1920–1939	−1.75[a]	−1.94[a]	−3.37[a]	−3.82[a]
Netherlands	1860–1879	−0.16[a]	+0.65[a]	−0.26[a]	+0.36[a]
	1880–1899	+3.15[a]	+0.80[a]	−2.64[a]	−3.94[a]
	1900–1919	+0.80[a]	−0.55[a]	−1.45[a]	−2.52[a]
	1920–1939	−1.69[a]	+0.83[a]	−1.58[a]	−1.44[a]
Norway	1860–1879	+3.41[a]	+4.27[a]	+1.64[a]	+1.95[a]
	1880–1899	+0.83[a]	−1.37[a]	−2.66[a]	−3.64[a]
	1900–1919	−0.14[a]	−1.22[a]	−1.54[a]	−2.53[a]
	1920–1939	−2.80[a]	−1.51[a]	−2.08[a]	−2.97[a]
Sweden	1860–1879	+1.99[a]	+2.87[a]	−0.39[a]	+1.11[a]
	1880–1899	−0.36[a]	−2.82[a]	−2.83[a]	−3.78[a]
	1900–1919	−0.69[a]	−1.93[a]	−1.35[a]	+2.59[a]
	1920–1939	−2.42[a]	−1.50[a]	−2.22[a]	−3.10[a]

Abbreviation: IHD, ischemic heart disease.
[a] Trends different from 0 with statistical significance ($P < 0.01$).

mortality and infant mortality was found in the different countries. On the other hand, there was a significant and strong positive association across birth cohorts between IMR and stroke mortality at adult age. The correlation coefficients were 0.83 for Denmark and 0.93 or more for other countries. When all countries are pooled, and associations across countries are also taken into account, the overall correlation is large for stroke (0.72) but nonsignificant for IHD mortality.

In Table 4, correlations across countries are calculated separately for each 5-year birth cohort. The relationship between stroke mortality and IMR was slightly positive when comparing countries for birth cohorts born before 1900. However, for birth cohorts born after 1900 this association was slightly negative. The inter-country association between IHD and infant mortality was negative in all birth cohorts, with significant negative correlations for birth cohorts born before 1895. Thus, countries with higher IMR before 1895 had lower IHD mortality rates among the same birth cohorts at adult ages.

Table 3
Correlation between trends in IHD or stroke mortality at adult ages and IMR among the birth cohorts from 1860 to 1939 in seven European countries

		Pearson correlation coefficient (95% CI)	
Country	Sex	IHD and IMR	Stroke and IMR
Denmark	Total	0.78 (0.46, 0.92)	0.83 (0.57, 0.94)
	Male	0.42 (−0.10, 0.76)	0.82 (0.55, 0.94)
	Female	0.89 (0.70, 0.96)	0.84 (0.59, 0.94)
England & Wales	Total	0.91 (0.76, 0.97)	0.93 (0.80, 0.97)
	Male	0.87 (0.65, 0.95)	0.93 (0.80, 0.98)
	Female	0.94 (0.84, 0.98)	0.93 (0.80, 0.97)
Finland	Total	0.28 (−0.27, 0.69)	0.95 (0.87, 0.99)
	Male	0.08 (−0.45, 0.57)	0.97 (0.91, 0.99)
	Female	0.54 (0.04, 0.83)	0.95 (0.86, 0.98)
France	Total	−0.20 (−0.64, 0.32)	0.95 (0.85, 0.98)
	Male	−0.32 (−0.70, 0.21)	0.95 (0.87, 0.98)
	Female	0.17 (−0.35, 0.62)	0.94 (0.84, 0.98)
Netherlands	Total	−0.86 (−0.95, −0.63)	0.97 (0.92, 0.99)
	Male	−0.86 (−0.95, −0.63)	0.97 (0.92, 0.99)
	Female	−0.64 (−0.86, −0.21)	0.97 (0.92, 0.99)
Norway	Total	0.23 (−0.30, 0.65)	0.98 (0.93, 0.99)
	Male	−0.18 (−0.62, 0.34)	0.98 (0.94, 0.99)
	Female	0.62 (0.17, 0.85)	0.98 (0.93, 0.99)
Sweden	Total	0.87 (0.66, 0.95)	0.99 (0.96, 1.00)
	Male	0.55 (0.07, 0.82)	0.99 (0.96, 1.00)
	Female	0.92 (0.77, 0.97)	0.98 (0.94, 0.99)
All Countries	Total	−0.08 (−0.55, 0.43)	0.72 (0.34, 0.90)
	Male	−0.18 (−0.62, 0.35)	0.72 (0.36, 0.90)
	Female	0.07 (−0.44, 0.55)	0.72 (0.34, 0.89)

Abbreviations: IHD, ischemic heart disease; IMR, infant mortality rate; CI, Confidence Interval.

4. Discussion

There have been relatively few studies on the possible impact of early life circumstances on trends in mortality from cardiovascular diseases within national populations.

Table 4
Correlation between international variations in IHD/Stroke mortality at adult ages and IMR for the birth cohorts from 1875 to 1925

	Pearson correlation coefficient (95% CI)	
Birth cohort	IHD and IMR	Stroke and IMR
1875–1879	−0.57 (−0.83, −0.11)	0.14 (−0.38, 0.59)
1880–1884	−0.65 (−0.86, −0.22)	0.18 (−0.35, 0.62)
1885–1889	−0.66 (−0.87, −0.24)	0.05 (−0.45, 0.54)
1890–1894	−0.62 (−0.85, −0.18)	0.07 (−0.44, 0.55)
1895–1899	−0.24 (−0.66, 0.29)	0.31 (−0.22, 0.70)
1900–1904	−0.31 (−0.70, 0.22)	−0.10 (−0.57, 0.41)
1905–1909	−0.24 (−0.66, 0.29)	−0.17 (−0.61, 0.36)
1910–1914	−0.18 (−0.62, 0.34)	−0.18 (−0.62, 0.34)
1915–1919	−0.20 (−0.63, 0.33)	−0.06 (−0.54, 0.45)
1920–1924	−0.23 (−0.65, 0.30)	−0.16 (−0.60, 0.37)

Abbreviations: IHD, ischemic heart disease; IMR, infant mortality rate; CI, Confidence Interval.

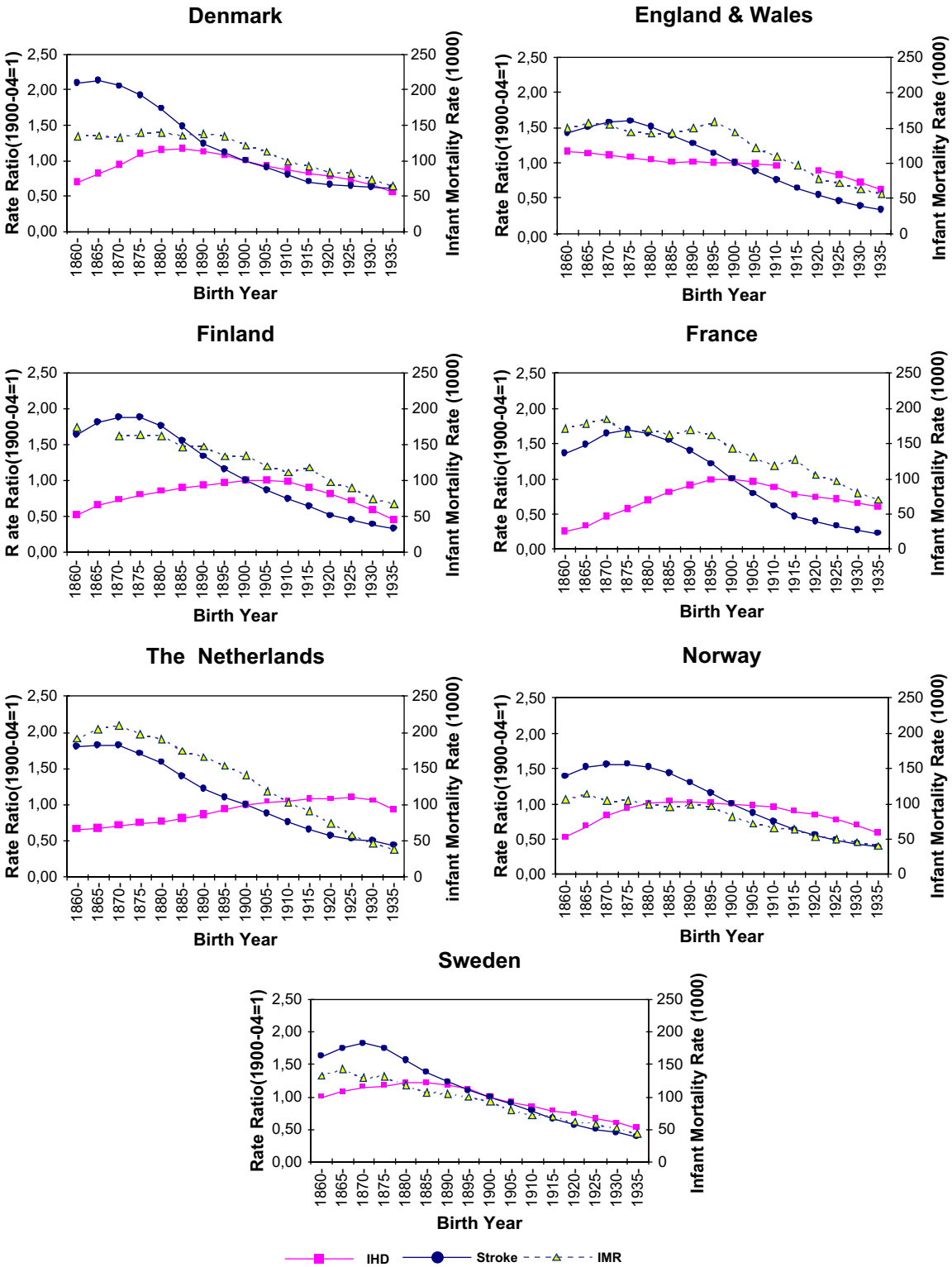

Fig. 1. Trends in IMR and in the mortality rate ratio of IHD and stroke at adult ages, in 5-year birth cohorts from 1860 to 1939.

We performed a time-series analysis in which special attention was paid to cohort patterns. We studied trends in IHD and stroke in relation to IMR in birth cohorts born between 1860 and 1939 in seven low-mortality European countries, observing a general cohort-wise decline in mortality from stroke in all countries and in both sexes, compared to an epidemic pattern of change for IHD. Although the trends in IHD mortality were not strongly correlated with the IMR in subsequent cohorts, strong and positive correlations were observed for stroke.

However, irregularities in trends in IMR between 1860 and 1940 were not reflected in similar irregularities in trends in stroke in later years. The irregularities in secular trends in IMR reflect true and important developments in the past, which might have been reflected in the mortality rates of affected birth cohorts during their later life. However, such lasting effects are not observed in our study. In addition, inter-country variations in IMR levels in the past had no strong positive correlations with cohort levels of stroke mortality at adult age.

We should stress that our objectives, empirical analyses, and inferences all refer to the same level of analyses, i.e., national populations. In this type of analysis, there is a risk of ecological fallacy [34]. However, this fallacy would be committed only if inferences were to be made toward the individual level. We have refrained from making such inferences, because trends in stroke mortality at the national level may strongly be influenced by factors that may have little effect at the individual level.

The mortality and population data used in this study come from data sources that are known to be of good quality [35–37]. Any problems with the coverage or completeness of death registries, or population registrations are likely to have had no or minimal effects on our results. We made a special effort to deal with ICD- and other coding related changes affecting mortality trends from IHD and stroke that are often neglected in other studies. Even though some residual effects of coding problems could not be excluded, we are confident that these problems did not affect the results to any substantial extent [28,29].

The results for the oldest 5-year cohorts (i.e., birth cohort 1860–1864) should be interpreted cautiously, as only the mortality of those aged 85 years and over could be studied. Therefore, no valid comparisons can be made between the mortality level of this cohort and the mortality levels of younger cohorts, in which the mortality at younger ages could also be studied. Greater weight should, therefore, be given to results for the birth cohorts that could be followed across a longer age range, i.e., cohorts born after 1870 or 1875.

The question is whether different results would have been obtained if the competing causes of death phenomenon had been taken into account. Due to the ''competing causes of death'' problem, the level of mortality from both causes of death may be lower than it would have been without competition for the lives of people with common risk factors. It is impossible to correct for this common phenomenon in our trend analysis [38]. The overall effect would have been an increase in the number of deaths observed for either cause of death, especially at the oldest ages. However, recent analyses have suggested that time trends in old-age mortality may not be affected very much by selection (or competition) effects for mortality at earlier ages [39]. Peeters et al., furthermore, concluded that there is no support for the hypothesis that increases in the number of people with cardiovascular disease, as a consequence of improvements in cardiovascular disease survival, explain the observed leveling off of the decline in the rate of stroke mortality [25].

The outcome measures in our study are mortality rates for IHD and stroke according to birth cohort and country. Differences in mortality rates by place and over time are the result of a complex interplay of many factors. In our analysis of associations with IMR, we were not able to control for potential confounders. For example, the cohort patterns of IHD mortality, which peaked among birth cohorts born around 1900, might be determined by smoking and other factors related to later phases of the life course. Similarly, the inverse (instead of positive) correlations between IMR and stroke in the cross-national analyses might have been confounded by cross-national differences in recent factors such as modern diet, alcohol consumption patterns, or hypertension treatment. Given this potential for confounding, the correlations observed in this study should be regarded as suggestions to be confirmed in future population-based studies.

The secular trends in IHD in the second half of the 20th century (an epidemic pattern) were very different from the steady decline in stroke. The factors that explain the different trends for IHD in comparison to stroke are not fully understood, but may be related to a relatively greater impact of smoking and serum cholesterol on IHD mortality compared to stroke mortality. Although IHD and stroke share key risk factors such as high blood pressure, tobacco use, and overweight [40,41], the strength and directions of the associations may be different for the two diseases. The discrepancy in trends for IHD and stroke warns against too strong statements regarding the effect of early living conditions.

Several reports have argued that declining IHD and stroke mortality rates are attributable to improved survival rates rather than to decreased incidence rates [42–46]. The declining case fatality [47] may be due to advances in diagnosis and treatment [48], including rapid dissemination of computed tomography (CT) and magnetic resonance imaging (MRI) technology since 1970s [49]. Studies on 10-year trends in the WHO MONICA (World Health Organization Monitoring of Cardiovascular Diseases) populations show that two thirds of the decline in stroke mortality remains unexplained after control for classical risk factors [50]. A part of the unexplained trends might be due to changes in other risk factors, such as socioeconomic status, food consumption, or different combinations of some or all of these [50]. Early life exposures might be one of the factors that contribute to trends in stroke mortality.

By understanding the process of growth development, and by scrutinizing the growth process, factors in early life that influence susceptibility to later disease can be identified [51]. van Rossum reported that risk factors earlier in life may be of importance in stroke [52]. Areas of England and Wales with high stroke mortality were characterized in the past by poor living standards, demonstrated by high

infant and maternal mortality rates, and short stature in the adult population [9]. Stroke may be related to maternal influences associated with poverty; this suggestion is supported by recent findings that rates of stroke in adult life are higher among people who had low birth weight [9]. Reduced fetal growth, i.e., the reduction in growth, which begins early in gestation, is associated with increased risk of cardiovascular disease [53].

To conclude, we observed a strong relationship between cohort-trends in stroke mortality and cohort-trends in infant mortality in European low-mortality countries. Although determining the exact contribution of living conditions in early life to national trends in stroke mortality remains difficult to ascertain, this association is in line with evidence from individual level studies. It suggests that living conditions earlier in life may have had an effect on the mortality experience of national cohorts, and that changes over time in these living conditions may have contributed to the secular decline in stroke mortality. We conclude that cohort patterns should be considered when studying secular trends in mortality from cardiovascular diseases. Future studies on the role of early life circumstances should be sensitive to differences between countries and between historical periods in the potential impact of these circumstances.

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